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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/096,648	06/12/1998	GYULA HADLACZKY	24601-402A	2049

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EXAMINER
TON, THAIAN N

ART UNIT	PAPER NUMBER
1632	32

DATE MAILED: 07/10/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/096,648	Applicant(s) HADLACZKY ET AL.	
	Examiner Thaian N. Ton	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 May 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-39,43,44,59,60,65,74,82-89,93-97,100 and 6771* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *98 and 99* is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *31* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/29/02, Paper No. 28, has been entered.

Applicants' Amendment, filed 6/3/02, Paper No. 30, has been entered.

Claims 33, 82 and 88 have been amended.

Claims 32-39, 43, 44, 59, 60, 65, 67, 71-74, 82-89, 93-100 are pending and under current examination.

Rejections made of record in the prior Office actions (Paper No. 24 & 26) not made of record in the instant Office action have been withdrawn in view of Applicants' arguments, amendments to the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The prior rejection of claims 32-39, 43, 44, 59, 60, 65, 67, 71-74, 82-89 and 93-97 and 100 are maintained for the reasons advanced on pages 3-4 of the final Office Action, mailed 11/26/01, Paper No. 24.

However, please note that the Perez Declaration under 37 CFR 1.132 filed February 1, 2001 (Paper No. 17) is sufficient with regard to the following enabled scope: a method for producing a transgenic non-human mammal comprising introducing in a female non-human mammal an ovum comprising a SATAC, wherein the ovum develops into a zygote or embryo; and allowing the embryo to develop into a transgenic non-human mammal comprising said SATAC; and a method for producing a transgenic mouse comprising introducing mouse embryonic stem cells comprising a SATAC into a mouse embryo and introducing said embryo into a female mouse; and allowing the embryo to develop into a transgenic mouse comprising said SATAC.

Applicants argue that although claims 98 and 99 are deemed allowable, the remainder of the claims, which were rejected in the final Office action, for missing critical steps dependent upon the source cell(s), however, Applicants argue that, "there are claims pending (i.e., claims 33, 34, 38, 39, 65, 71, 85-89 and 97) which specify a cell containing an artificial chromosome is a fertilized ovum, zygote, embryo, or mouse embryonic stem cell and that are not within the purview of the rejection." Applicants further argue that specific claims, such as 33, 65, 71 and 87 specific the cell comprising an artificial chromosome is either a fertilized ovum or mouse ES cell [see p. 3, last paragraph of the Response]. Applicants further ague

that claims 34, 88, 89 and 97 specify that the cell containing the artificial chromosome is an embryo or an embryo containing the artificial chromosome, which would be introduced into a female non-human mammal; that claim 39 specifies a cell containing an artificial chromosome as a zygote; that claims 38, 85 and 86 specify that the artificial chromosome is contained in a pronucleus [i.e., fertilized egg]. Applicants conclude that because the above-cited claims all recite cells or embryos which are compositions identified in the final Office action as sufficient for the development into an animal, there is no other basis on which the claims are rejected [see p. 4 of the Response].

Applicants' arguments have been considered but they are not found persuasive. In particular, it is reiterated that the independent claims 32, 43, 44, 73, 74, 82, 93, 95, and 96 recite the term, "cell(s)". Although dependent claims further distinguish the particular "cell(s)", as noted by Applicant in the Response, all claims have been included in this rejection, as the claims are not complete because the claims are missing critical steps dependent upon the source "cell(s)". (See scope of enablement, above). Although dependent claims do further limit and distinguish particular cells that are sufficient with regard to the enabled scope, the invention as broadly claimed encompasses any type of cell(s), and the introduction of an artificial chromosome into these cell(s) as broadly claimed, would not be sufficient to produce any animal.

Applicants argue that the claims are complete without a recitation of fertilization or a fertilized cell, that Applicants have provided exemplary cells for

use in the claimed invention, and that one of skill in the art could readily determine a number of cells that would be used in the claimed methods [see p. 6, 1st paragraph of the Response]. Applicants direct the examiner to Campbell *et al.*, who teach nuclear transfer methods for the generation of transgenic animals. Particularly, Applicants argue that nuclear transfer does not require a fertilized oocyte, therefore fertilization would not be essential to the claimed methods, and as such, the claims are not missing critical steps, but are complete as written. Applicants further argue that transgenic embryos and animals of can be produced using satellite artificial chromosomes whether or not the presence of such chromosomes constitutes "correct ploidy". In particular, Applicants argue that it is not clear what is mean by "correct" ploidy, and further, that the Examiner has not provided any evidence or technical reasoning to support the requirement of correct ploidy for nuclear transfer techniques. Further, Applicants argue that even if the lack of correct ploidy would occur if a satellite artificial chromosome is present in the cell, it is a condition that would occur irrespective of the method used in the production of the transgenic animal. [See p. 8 of the Response].

The Campbell references have been carefully considered. With Applicants' interpretation of the Examiner's for the requirement for a fertilized oocyte, the Examiner disagrees that the prior Office actions state that the claimed methods require a fertilized oocyte. The Examiner presents the example of an unfertilized oocyte that would not develop into an animal if utilized in the broadly claimed methods. Particularly, as the claimed methods do not recite nuclear transfer steps,

merely introduction of an artificial chromosome into any particular type of cell, for example, an unfertilized oocyte, would not predictably result in the development of a transgenic animal, see also *supra.* Furthermore, the Examiner notes it is well-known in the art although nuclear transfer techniques do not require a fertilized oocyte, however, nuclear transfer would require the correct chromosomal number, or ploidy, which would not be present if a SATAC were present. For example, it is well-known that in development that incorrect chromosomal number in the developing fetus often does not result in a live-born offspring. Furthermore, it is noted that the claimed invention is enabled for an "ovum" that develops into a zygote or embryo [see *supra*], it is noted that an "ovum" does not refer to a fertilized egg. Additionally, it is noted that the claimed invention, as broadly written, is not particular to nuclear transfer methods, nor to particular cells that would be predictably expected to produce transgenic mammals of the claimed method and as such, it is maintained that the claims are not complete because the claims are missing critical steps dependent upon the source cell(s).

Applicants argue that even if there is a possibility that not every cell would yield an embryo or animal in the method of transgenic animal production, it would not invalidate a claim that does not specify a particular cell type. Applicants argue that what is relevant to the scope of enablement is that there are number of cells, so of which are explicitly listed in the application and others that would be known to those of skill in the art based upon the combination of the teachings of the application and what was known in the art at the time of filing of the application,

that will develop into an embryo and a mammal, and therefore the claims need not specify the cell type in order to be enabled and definite [see p. 9, 2nd paragraph of the Response].

In response, it is noted that the enabled scope of the claimed invention is not only based upon the teachings, evidence and guidance provided by the specification, but additionally by the state of the art. It is art-recognized that only particular cells would be capable of developing into a transgenic non-human mammal. The claims, as broadly written, read on any cell type, and although further dependent claims limit the cell types, it is noted, as *supra* that the claims are not complete because they are missing critical steps which are dependent upon the source cell(s). Accordingly, in view of the state of the art, and the lack of guidance or teachings provided by the specification for the generation of transgenic non-human mammals by the introduction into any cell an artificial chromosome and allowing the cell to develop into a transgenic non-human mammal, the claimed invention is only enabled for a method for producing a transgenic non-human mammal comprising introducing in a female non-human mammal an ovum comprising a SATAC, wherein the ovum develops into a zygote or embryo; and allowing the embryo to develop into a transgenic non-human mammal comprising said SATAC; and a method for producing a transgenic mouse comprising introducing mouse embryonic stem cells comprising a SATAC into a mouse embryo and introducing said embryo into a female mouse; and allowing the embryo to develop into a transgenic mouse comprising said SATAC.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32-39, 43, 44, 59, 60, 65, 67, 71-74, 82-89 and 93-97 and 100 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is maintained that the claims, as written are incomplete. See p. 5 of final Office Action (Paper No. 24). Applicants argue that the essential steps of the method claims have been provided in the currently pending claims (see p. 13), however, Applicants' amendments to the claims fail to overcome this rejection. For example, claims 32, 43, 44, 73, 74, 82, 93, 95, and 96 recite the term, "cell(s)". Dependent claims further distinguish the particular "cell(s)". As such, all claims have been included in this rejection, as the claims are not complete because the claims are missing critical steps dependent upon the source "cell(s)".

Applicants argue that the final Office action directs the Applicants' attention to the, "scope of enablement" and thus that the same rejection of the claims is being made under 112 1st as under 112, 2nd.

The Examiner disagrees. The rejection of the claimed invention under 112, 1st paragraph is directed to the enablement of the claims, whereas the 112 2nd paragraph rejection is based upon the fact that claims are incomplete because

essential method steps are missing. For example, in claim 32, it is huge leap to go from the introduction of an artificial chromosome into a cell to the development of a transgenic mammal. Particularly as more is required, including essential steps, such as introducing an ES cell or fertilized ovum, for example, transplanting the embryo into a recipient non-human mammal, allow the embryo to develop to term, and identifying the transgenic non-human mammal whose genome comprises a SATAC. It is noted that this rejection was set forth in Office action mailed 6/21/00, Paper No. 12, and further clarified in the final Office action, mailed 11/26/01, Paper No. 24.

Conclusion

Claims 98 and 99 are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thaian N. Ton whose telephone number is (703) 305-1019. The examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off. Should the examiner be unavailable, inquiries should be directed to Deborah Reynolds, Supervisory Primary Examiner of Art Unit 1632, at (703) 305-4051. Any administrative or procedural questions should be directed to Patsy Zimmerman, Patent Analyst, at (703) 305-2758. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-8724.

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